

What is claimed is:

1. 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-hydrazono]-5-methyl-2,4-dihydropyrazol-3-one choline.

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2. A pharmaceutical composition comprising 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-hydrazono]-5-methyl-2,4-dihydropyrazol-3-one choline and a pharmaceutically acceptable carrier or diluent.

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3. A method of treating thrombocytopenia in a mammal in need thereof which comprises administering to such mammal a therapeutically effective amount of a compound as described in claim 1.

4. A method as claimed in claim 3, wherein the mammal is a human.

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5. A method of enhancing platelet production in a mammal in need thereof which comprises administering to such mammal a therapeutically effective amount of a compound as described in Claim 1.

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6. A method as claimed in claim 5, wherein the mammal is a human.

7. The method of claim 3 wherein the compound is administered orally.

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8. The method of claim 3 wherein the compound is administered parenterally.

9. A method of agonizing the TPO receptor in a subject which comprises administering an effective amount of a compound as described in claim 1.

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10. A process for preparing a pharmaceutical composition containing a pharmaceutically acceptable carrier or diluent and an effective amount of a compound as described in claim 1, which process comprises bringing the compound described in claim 1 into association with the pharmaceutically acceptable carrier or diluent.

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11. The method of Claim 3 further comprising co-administering a therapeutically effective amount of an agent selected from the group consisting of: a

colony stimulating factor, cytokine, chemokine, interleukin or cytokine receptor agonist or antagonists, soluble receptors, receptor agonists or antagonist antibodies, or small molecules or peptides that act by the same mechanisms of one or more of said agents.

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12. The method of Claim 11 wherein the agent is selected from the group consisting of: G-CSF, GM-CSF, TPO, M-CSF, EPO, Gro-beta, IL-11, SCF, FLT3 ligand, LIF, IL-3, IL-6, IL-1, Progenipoinetin, NESF, SD-01, IL-8, or IL-5 or a biologically active derivative of any of said agents.

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13. A pharmaceutical composition of Claim 2 further comprising co-administering a therapeutically effective amount of an agent selected from the group consisting of: a colony stimulating factor, cytokine, chemokine, interleukin or cytokine receptor agonist.

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14. The composition of Claim 13 wherein the agent is selected from the group consisting of: G-CSF, GM-CSF, TPO, M-CSF, EPO, Gro-beta, IL-11, SCF, FLT3 Ligand, LIF, IL-3, IL-6, IL-1, or IL-5 or a biologically active derivative of any of said agents.

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15. A method for enhancing platelet production obtained from a donor which comprises administering to such donor a therapeutically effective amount of a compound as described in Claim 1 prior to platelet pheresis, blood donation or platelet donation.

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16. A method for enhancing the number of peripheral blood stem cells obtained from a donor which comprises administering to such donor a therapeutically effective amount of a compound as described in Claim 1 prior to leukapheresis.

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17. A method of Claim 16 further comprising co-administering a therapeutically effective amount of a hematopoietic-cell mobilizing agent selected from the group consisting of: a colony stimulating factor, cytokine, chemokine, interleukin or cytokine receptor agonist, adhesion molecule antagonists or antibodies.

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18. The method of Claim 17 wherein the mobilizing agent is selected from the group consisting of: G-CSF, GM-CSF, TPO, EPO, Gro-beta, IL-8, cytoxan, VLA-

4 inhibitors, SCF, FLT3 ligand or a biologically active derivative of G-CSF, GM-CSF, TPO, EPO, Gro-beta or IL-8.

5 19. An in vitro or ex vivo method for enhancing stimulation of megakaryocyte maturation and/or platelet production which comprises adding an effective amount of a compound as described in Claim 1 to the culture medium of cells that express the TPO receptor.

10 20. An in vitro or ex vivo method for enhancing stimulation of megakaryocyte maturation and/or platelet production which comprises adding an effective amount of a compound as described in Claim 1 to the culture medium of stem cells, bone marrow cells, cord-blood cells or peripheral blood cells.

15 21. A method of claim 20, wherein the megakaryocytes or platelets are returned to the mammal following chemotherapy or radiation therapy.

20 22. An in vitro or ex vivo method for enhancing the survival and/or proliferation of stem cells, bone marrow cells, cord-blood cells, peripheral blood cells or other types of cells expressing the TPO receptor in culture which comprises culturing said cell in a medium containing an effective amount of a compound as described in Claim 1.

25 23. A method of claim 22 further comprising co-administration of a therapeutically effective amount of a colony stimulating factor, cytokine, chemokine, interleukin or cytokine receptor agonist.

24. A method of claim 22 wherein the stem cells are returned to the mammal following chemotherapy or radiation therapy.

30 25. A method of treating neutropenia in a mammal, including a human, in need thereof which comprises administering to such mammal a therapeutically effective amount of a compound as described in claim 1.

35 26. An in vitro or ex vivo method for enhancing stimulation of neutrophil production which comprises adding an effective amount of a compound as described in Claim 1 to the culture medium of stem cells, bone marrow cells, cord-blood cells, peripheral blood cells or other types of cells expressing the TPO receptor.

27. A method of claim 26, wherein the neutrophils are returned to the mammal following chemotherapy or radiation therapy.

5 28. A method of claim 3 wherein said thrombocytopenia is due to myelosuppression caused by chemotherapy or radiation therapy.

29. A method of claim 3 wherein said thrombocytopenia is due to an organ transplant.

10 30. A method of claim 3 wherein said thrombocytopenia is due to bone marrow, stem cell, or liver transplant.

31. A method of claim 3 wherein said thrombocytopenia is due to idiopathic thrombocytopenia purpura (ITP).

32. A method of claim 3 wherein said thrombocytopenia is due to myelodysplastic syndromes (MDS), aplastic anemia or leukemia.

20 33. A method of claim 3 wherein said thrombocytopenia is due to viral, fungal, microbial or parasitic infection.

34. A method of claim 3 wherein said thrombocytopenia is due to liver dysfunction.

25 35. A method of claim 3 wherein said thrombocytopenia is due to surgical procedures.

36. A method of claim 3 wherein said thrombocytopenia is drug – induced.

30 37. A process for preparing the compound of claim 1, which process comprises:

35 i) dissolving 2-(3,4-dimethylphenyl)-4-{{[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-hydrazono}-5-methyl-2,4-dihydropyrazol-3-one in an organic solvent or solvents, to form a solution;

 ii) adding one or more equivalents of choline hydroxide to the solution; and

iii) isolating the prepared compound.

38. A method of treating a degenerative disease in a mammal in need thereof which comprises the in vivo administration of a therapeutically effective
5 amount of a compound of claim 1 to such mammal.

39. A method as claimed in claim 38 wherein the mammal is a human.

40. The method of claim 38 wherein the degenerative disease is selected
10 from: transverse myelitis, multiple sclerosis, demyelination occurring after trauma to the brain or spinal cord, acute brain injury, head trauma, spinal cord injury, peripheral nerve injury, ischaemic brain injury, hereditary myelin disorder of the CNS, epilepsy, perinatal asphyxia, asphyxia, anoxia, status epilepticus, stroke, Alzheimer's disease, Parkinson disease, Huntington's disease, amyotrophic lateral sclerosis,
15 cardiovascular disorder, myocardial infarction, cardiovascular disease, liver disease, gastrointestinal disease, kidney disease, AIDS, diabetes and diabetes mellitus.

41. The method of claim 38 wherein the degenerative disease is a
20 degenerative neural disease.

42. The method of claim 40 wherein the compound is administered orally.

43. The method of claim 40 wherein the compound is administered
25 parenterally.

44. A method of Claim 40 further comprising co-administering a
therapeutically effective amount of an agent selected from the group consisting of: a
colony stimulating factor, cytokine, chemokine, interleukin or cytokine receptor
agonist or antagonists, soluble receptors, receptor agonists or antagonist antibodies,
30 or small molecules or peptides that act by the same mechanisms one or more of said
agents.

45. The method of Claim 44 wherein the agent is selected from the group
consisting of: G-CSF, GM-CSF, TPO, M-CSF, EPO, Gro-beta, IL-11, SCF, FLT3
35 ligand, LIF, IL-3, IL-6, IL-1, Progenipoiectin, NESP, SD-01, IL-8, or IL-5 or a
biologically active derivative of any of said agents.

46. The method of Claim 40 further comprising co-administering a therapeutically effective amount of a hematopoietic-cell mobilizing agent selected from the group consisting of: a colony stimulating factor, cytokine, chemokine, interleukin or cytokine receptor agonist, adhesion molecule antagonists or
5 antibodies.

47. The method of Claim 46 wherein the mobilizing agent is selected from the group consisting of: G-CSF, GM-CSF, TPO, EPO, Gro-beta, IL-8, cytoxan, VLA-4 inhibitors, SCF, FLT3 ligand or a biologically active derivative of G-CSF, GM-CSF,
10 TPO, EPO, Gro-beta or IL-8.

48. A method of claim 40 wherein the degenerative disease is due to viral, fungal, microbial or parasitic infection.

15 49. A method of claim 40 wherein the degenerative disease is due to liver dysfunction.

50. A method of claim 40 wherein the degenerative disease is due to surgical procedures.
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51. A method of claim 40 wherein the degenerative disease is due to treatment with antiviral or antibiotic agents.

25 52. A method of claim 40 wherein the degenerative disease is due a spinal cord injury.

53. A method of treating a diseases state selected from: transverse myelitis, multiple sclerosis, demyelination occurring after trauma to the brain or spinal cord, acute brain injury, head trauma, spinal cord injury, peripheral nerve injury, ischaemic brain injury, hereditary myelin disorder of the CNS, epilepsy, perinatal asphxia, asphyxia, anoxia, status epilepticus, stroke, Alzheimer's disease, Parkinson disease, Huntington's disease, amyotrophic lateral sclerosis, cardiovascular disorder, myocardial infarction, cardiovascular disease, liver disease, gastrointestinal disease, kidney disease, AIDS, diabetes and diabetes mellitus, which comprises the in vivo
30 administration an effective amount of a compound of claim 1.
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54. A method of treating a degenerative neural disease which comprises the in vivo administration of an effective amount of a compound as described in claim 1.

55. A method of treating a diseases state selected from: transverse myelitis, multiple sclerosis, demyelination occurring after trauma to the brain or spinal cord, acute brain injury, head trauma, spinal cord injury, peripheral nerve injury, ischaemic brain injury, hereditary myelin disorder of the CNS, epilepsy, perinatal asphxia, asphyxia, anoxia, status epilepticus, stroke, Alzheimer's disease, Parkinson disease, Huntington's disease, amyotrophic lateral sclerosis, cardiovascular disorder, myocardial infarction, cardiovascular disease, liver disease, gastrointestinal disease, kidney disease, AIDS, diabetes and diabetes mellitus, which comprises the in vivo administration of an effective amount of a composition as described in claim 2.

56. A method of treating a degenerative neural disease which comprises the in vivo administration of an effective amount of a compound as described in claim 2.

57. A method of treating a degenerative disease in a mammal in need thereof which comprises the administration of a therapeutically effective amount of the compound of claim 1 to such mammal.

58. The method of claim 57 wherein the mammal is a human.

59. The process of claim 37 wherein the solution contains a mixture of ethyl acetate and ethanol.

60. The process of claim 37 wherein the solution contains tetrahydrofuran.